AMENDMENTS TO THE SPECIFICATION

Please replace the paragraph beginning at page 76, line 34, with the following rewritten paragraph:

Sequences identified in such library screening methods can be compared and aligned to other known sequences deposited and available in public databases such as ~~GenBank~~GENBANK database or other private sequence databases. Sequence identity (at either the amino acid or nucleotide level) within defined regions of the molecule or across the full-length sequence can be determined using methods known in the art and as described herein.

Please replace the paragraph beginning at page 99, line 20, with the following rewritten paragraph:

The extracellular domain (ECD) sequences (including the secretion signal sequence, if any) from about 950 known secreted proteins from the Swiss-Prot public database were used to search EST databases. The EST databases included public databases (e.g., ~~Dayhoff, GenBank~~DAYHOFF database,GENBANK database) and proprietary databases (e.g. LIFESEQ™ ® database, Incyte Pharmaceuticals, Palo Alto, Calif.). The search was performed using the computer program BLAST or BLAST-2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)) as a comparison of the ECD protein sequences to a 6 frame translation of the EST sequences. Those comparisons with a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into consensus DNA sequences with the program "phrap" (Phil Green, University of Washington, Seattle, Wash.).

Please replace the paragraph beginning at page 103, line 6, with the following rewritten paragraph:

Various polypeptide-encoding nucleic acid sequences were identified by applying a proprietary signal sequence finding algorithm developed by Genentech, Inc. (South San Francisco, Calif.) upon ESTs as well as clustered and assembled EST fragments from public (e.g., ~~GenBank~~GENBANK database) and/or private (LIFESEQ® database, Incyte Pharmaceuticals, Inc., Palo Alto, Calif.) databases. The signal sequence algorithm computes a secretion signal score based on the character of the DNA nucleotides surrounding the first and optionally the second methionine codon(s) (ATG) at the 5'-end of the sequence or sequence fragment under consideration. The nucleotides following the first ATG must code for at least 35 unambiguous amino acids without any stop codons. If the first ATG has the required amino acids, the second is not examined. If neither meets the requirement, the candidate sequence is not scored. In order to determine whether the EST sequence contains an authentic signal sequence, the DNA and corresponding amino acid sequences surrounding the ATG codon are scored using a set of seven sensors (evaluation parameters) known to be associated with

secretion signals. Use of this algorithm resulted in the identification of numerous polypeptide-encoding nucleic acid sequences.

Please replace the paragraph beginning at page 103, line 20, with the following rewritten paragraph:

PRO196 was identified by screening the ~~GenBank~~GENBANK database using the computer program BLAST (Altshul et al., Methods in Enzymology 266:460-480 (1996). The PRO196 sequence shows homology with known expressed sequence tag (EST) sequences T35448, T11442, and W77823. None of the known EST sequences have been identified as full length sequences, or described as ligands associated with the TIE receptors.

Please replace the sentences beginning at page 103, line 31, with the following rewritten sentences:

based on the ESTs found in the ~~GenBank~~GENBANK database. cDNA sequences were sequenced in their entireties.

Please replace the paragraph beginning at page 104, line 19, with the following rewritten paragraph:

DNA molecules encoding the PRO183, PRO185, PRO9940, PRO2630 and PRO6309 polypeptides shown in the accompanying figures were obtained through ~~GenBank~~the GENBANK database.

Please replace the paragraph beginning at page 108, line 13, with the following rewritten paragraph:

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated ~~Incyte cluster sequence~~ INCYTE CLUSTER SEQUENCE 10685. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., ~~GenBank~~GENBANK database) and a proprietary EST DNA database (~~Lifeseq~~LIFESEQ database, Incyte Pharmaceuticals, Palo Alto, Calif.) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST program score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Wash.). The consensus sequence obtained therefrom is herein designated DNA58839.

Please replace the paragraph beginning at page 110, line 10, with the following rewritten paragraph:

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., ~~GenBank~~GENBANK database) and a proprietary EST DNA database (LIFESEQ[[™]]® database[[.]], Incyte Pharmaceuticals, Palo Alto, Calif.) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST program score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Wash.). The consensus sequence obtained therefrom is herein designated DNA56037.

Please replace the paragraph beginning at page 111, line 1, with the following rewritten paragraph:

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., ~~GenBank~~GENBANK database) and a proprietary EST DNA database (LIFESEQ® database, Incyte Pharmaceuticals, Palo Alto, Calif.) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST program score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Wash.). The consensus sequence obtained therefrom is herein designated DNA58753.

Please replace the paragraph beginning at page 111, line 28, with the following rewritten paragraph:

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., ~~GenBank~~GENBANK database) and a proprietary EST DNA database (LIFESEQ® database, Incyte Pharmaceuticals, Palo Alto, Calif.) to identify existing homologies. One or more of the ESTs was derived from a diseased tonsil tissue library. The homology search was performed using the computer program BLAST or BLAST2 (Altshul

et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST program score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Wash.). The consensus sequence obtained therefrom is herein designated DNA59761.

Please replace the paragraph beginning at page 113, line 11, with the following rewritten paragraph:

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the LIFESEQ® database, Incyte Pharmaceuticals, Palo Alto, designated herein as CLU57836. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., ~~Genbank~~GENBANK database) and a proprietary EST DNA database (LIFESEQ® database, Incyte Pharmaceuticals, Palo Alto, Calif.) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST program score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Wash.). The consensus sequence obtained therefrom is herein designated DNA58756.

Please replace the paragraph beginning at page 116, line 17, with the following rewritten paragraph:

The EST sequence accession number AF007268, a murine fibroblast growth factor (FGF-15) was used to search various public EST databases (e.g., ~~GenBank~~GENBANK database, ~~Dayhoff~~DAYHOFF database, etc.). The search was performed using the computer program BLAST or BLAST2 [Altschul et al., Methods in Enzymology, 266:460-480 (1996)] as a comparison of the ECD protein sequences to a 6 frame translation of the EST sequences. The search resulted in a hit with ~~GenBank~~ EST AA220994 from the GENBANK database, which has been identified as stratagene NT2 neuronal precursor 937230.

Please replace the paragraph beginning at page 116, line 23, with the following rewritten paragraph:

Based on the ~~Genbank~~GENBANK database EST AA220994 sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence. Forward and reverse PCR primers may range from 20 to 30 nucleotides (typically about 24), and are designed to give a PCR

product of 100-1000 bp in length. The probe sequences are typically 40-55 bp (typically about 50) in length. In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification, as per Ausubel et al., Current Protocols in Molecular Biology, with the PCR primer pair. A positive library was then used to isolate clones encoding the gene of interest using the probe oligonucleotide and one of the PCR primers.

Please replace the paragraph beginning at page 119, line 19, with the following rewritten paragraph:

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from an Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., ~~GenBank~~GENBANK database) and a proprietary EST DNA database (LIFESEQ® database, Incyte Pharmaceuticals, Palo Alto, Calif.) to identify existing homologies. One or more of the ESTs were derived from a thryroid tissue library. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST program score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Wash.). The consensus sequence obtained therefrom is herein designated DNA56013.

Please replace the paragraph beginning at page 123, line 14, with the following rewritten paragraph:

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated herein as 5086173H1. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., ~~GenBank~~GENBANK database) and a proprietary EST DNA database (LIFESEQ® database, Incyte Pharmaceuticals, Palo Alto, Calif.) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST program score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Wash.). The consensus sequence obtained therefrom is herein designated DNA110880.

Please replace the paragraph beginning at page 129, line 16, with the following rewritten paragraph:

Twelve micrograms of the desired plasmid DNA is introduced into approximately 10 million CHO cells using commercially available transfection reagents ~~Superfect~~SUPERFECT. (Quiagen), ~~Dosper~~DOSPER or ~~Fugene~~FUGENE. (Boehringer Mannheim). The cells are grown as described in Lucas et al., supra. Approximately 3 x 10^{-7} cells are frozen in an ampule for further growth and production as described below.

Please replace the paragraph beginning at page 131, line 3, with the following rewritten paragraph:

Recombinant baculovirus is generated by co-transfecting the above plasmid and ~~BaculoGold~~BACULOGOLD™ virus DNA (Pharmingen) into Spodoptera frugiperda ("Sf9") cells (ATCC CRL 1711) using lipofectin (commercially available from GIBCO-BRL). After 4 -5 days of incubation at 28°C, the released viruses are harvested and used for further amplifications. Viral infection and protein expression are performed as described by O'Reilley et al., Baculovirus expression vectors: A Laboratory Manual, Oxford: Oxford University Press (1994).

Please replace the paragraph beginning at page 147, line 44, with the following rewritten paragraph:

The starting material for the screen was genomic DNA isolated from a variety cancers. The DNA is quantitated precisely, e.g., fluorometrically. As a negative control, DNA was isolated from the cells of ten normal healthy individuals which was pooled and used as assay controls for the gene copy in healthy individuals (not shown). The 5' nuclease assay (for example, ~~TaqMan~~TAQMAN™ assay.) and real-time quantitative PCR (for example, ABI ~~Prizm 7700 Sequence Detection System~~PRIZM 7700 SEQUENCE DETECTION SYSTEM™. (Perkin Elmer, Applied Biosystems Division, Foster City, Calif.)), were used to find genes potentially amplified in certain cancers. The results were used to determine whether the DNA encoding the PRO polypeptide is over-represented in any of the primary lung or colon cancers or cancer cell lines or breast cancer cell lines that were screened. The primary lung cancers were obtained from individuals with tumors of the type and stage as indicated in Table 8. An explanation of the abbreviations used for the designation of the primary tumors listed in Table 8 and the primary tumors and cell lines referred to throughout this example are given below.

Please replace the paragraph beginning at page 148, line 8, with the following rewritten paragraph:

The results of the ~~TaqMan~~TAQMAN™ assay are reported in delta (Δ) Ct units. One unit corresponds to 1 PCR cycle or approximately a 2-fold amplification relative to normal, two units corresponds to 4-fold, 3 units to 8-fold amplification and so on. Quantitation was obtained using primers and a ~~TaqMan~~TAQMAN™ fluorescent probe derived from the PRO polypeptide-encoding gene. Regions of the PRO polypeptide-encoding gene which are most likely to contain unique nucleic acid sequences and which are least likely to have spliced out introns are preferred for the primer and probe derivation, e.g., 3'-untranslated regions. The sequences for the primers and probes (forward, reverse and probe) used for the PRO polypeptide gene amplification analysis were as follows:

Please replace the paragraph beginning at page 149, line 5, with the following rewritten paragraph:

The 5' nuclease procedure is run on a real-time quantitative PCR device such as the ABI ~~Prism 7700TM Sequence Detection~~ PRIZM 7700 SEQUENCE DETECTION SYSTEM. The system consists of a thermocycler, laser, charge-coupled device (CCD) camera and computer. The system amplifies samples in a 96-well format on a thermocycler. During amplification, laser-induced fluorescent signal is collected in real-time through fiber optics cables for all 96 wells, and detected at the CCD. The system includes software for running the instrument and for analyzing the data.

Please replace the paragraph beginning at page 152, line 31, with the following rewritten paragraph:

The fluorometricly determined concentration was then used to dilute each sample to 10 ng/gl in ddH_2O. This was done simultaneously on all template samples for a single ~~TaqMan~~ TAQMAN™ plate assay, and with enough material to run 500-1000 assays. The samples were tested in triplicate with ~~Taqman~~TAQMAN™ primers and probe both B-actin and GAPDH on a single plate with normal human DNA and no-template controls. The diluted samples were used provided that the CT value of normal human DNA subtracted from test DNA was +/- 1 Ct. The diluted, lot-qualified genomic DNA was stored in 1.0 ml aliquots at -80°C. Aliquots which were subsequently to be used in the gene amplification assay were stored at 4°C. Each 1 ml aliquot is enough for 8-9 plates or 64 tests.

Please replace the paragraph beginning at page 155, line 22, with the following rewritten paragraph:

This assay is designed to identify gene expression patterns in pericytes induced by the hits in assay 93 described above. Bovine pericytes are plated on 60 mm culture dishes in growth media for 1 week. On day 1, various PRO polypeptides are diluted (1%) and incubated with the pericytes for 1, 4 and 24 hr. timepoints. The cells are harvested and the RNA isolated using TRI-Reagent following the included instructions. The RNA is then quantified by reading the 260/280 OD using a spectrophotometer. The gene expression analysis is done by ~~TaqMan~~TAQMAN™ reactions using Perkin Elmer reagents and specially designed bovine probes and primers. Expression of the following genes is analyzed: GAPDH, beta-integrin, connective tissue growth factor (CTGF), ICAM-1, monocyte chemoattractant protein-1 (MCP-1), osteopontin, transforming growth factor-beta (TGF-beta), TGF-beta receptor, tissue inhibitor of metalloproteinase (TIMP), tissue factor (TF), VEGF-.alpha., thrombospondin, VEGF-.beta., angiopoeitin-2, and collagenase. Replicates are then averaged and the SD determined. The gene expression levels are then normalized to GAPDH. These are then normalized to the expression levels obtained with a protein (PIN32) which does not significantly induce gene expression in bovine pericytes when compared to untreated controls. Any PRO polypeptide that gives a gene expression level 2-fold or higher over the PIN32 control is considered a positive hit.